UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,337	12/29/2003	Mark H. Tuszynski	041673-2115	9488

30542 7590 12/14/2005

FOLEY & LARDNER LLP
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/748,337	**Applicant(s)** TUSZYNSKI, MARK H.	
	Examiner Louis D. Lieto	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 November 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☒ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *1-8,11,12,14-18*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
    See Continuation Sheet.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 11/08/05
13. ☒ Other: See Continuation Sheet.

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800

Continuation of 11. does NOT place the application in condition for allowance because:

The rejection of claims 1-8, 11-12 and 14-18 under 35 USC 112 First paragraph for new matter is maintained for reasons of record as stated in the office action of 9/08/05. Applicant's arguments have been considered but were not found to be persuasive in overcoming this rejection. Applicant argues that their initial claim set is similar to a numerical range limitation as discussed in the cited case of In re Wertheim. However, in the instant case the range disclosed is an open-ended range of one, to a potentially infinite number of injection sites in the brain. This differs from the closed range discussed in In re Wertheim. As previously stated the specification does not clearly contemplate the specific limitation of "two or more delivery sites in the brain." Therefore it is still considered to be new matter.

The rejection of claims 1-8, 11-12 and 14-17 under 35 USC 112 First paragraph for lack of full scope of enablement is withdrawn in view of applicant's arguments.

The rejection of claim 18 under 35 USC 112 First paragraph for lack of full scope of enablement is maintained for reasons of record as stated in the office actions of 1/19/05 and 9/08/05. Applicant's arguments were not found to be persuasive in overcoming the prior grounds of rejection. As previously stated:

Claim 18 is specifically drawn to the treatment of Parkinson's disease in the human. However applicant has not disclosed any evidence in the specification that the claimed method can be used to treat Parkinson's disease in the human. The declaration of Mark Tuszynski discloses the effects of using the claimed method in animal models of Parkinson's disease, and indicates that adeno-associated viral vectors have been used to deliver neurotrophins into the brains of humans. However, no evidence is disclosed if the humans used in said experiments had or Parkinson's disease, what specific adeno-associated viral vectors encoded neurotrophins were delivered and if the humans were so afflicted what the efficacy of the treatment was. While the animal models used may have been the best available in the art at the time of invention, it is noted that neither the specification nor the art of record indicates that these models were predicative of the efficacy of a gene therapy treatment method for Parkinson's disease in humans. See also pages 5 and 6 of the office action of 1/19/2005. Applicant has not provided sufficient evidence to enable the skilled practitioner in the art to predict how to practice the claimed invention as a method of treatment for Parkinson's disease in humans, without undue and extensive experimentation.

In regards to applicant supplied references of Tuszynski et al. and the reports from the Chicago Tribune and the San Diego Tribune it is noted that these are all recent post-filing references that do not describe treatments of Parkinson's disease. The rejection is maintained for reasons of record as stated above and in the office actions of 1/19/05 and 9/08/05.

Claims 1 and 2 remain rejected under 35 U.S.C. 102(b) as being anticipated by Martinez-Serrano et al. { Martinez-Serrano et al. (1995) J. Neuroscience 15:5668-5680}

As previously stated:

Martinez-Serrano et al. provides guidance on a method of administering a therapeutic neurotrophin composition, comprising a neural progenitor cell line transfected with a MMLV retrovirus encoding a mouse NGF cDNA into the brain of a rodent in more than one location (pgs. 5669-5671). Martinez-Serrano et al. teaches delivering the neural progenitor cell line to two locations no more than about 10mm apart (pg. 5670, Materials and Methods). Further, Martinez-Serrano et al. teaches that the engrafted cells blocked over 90% of the cholinergic cell loss in fimbria-fornix induced lesions (Abstract; pg 5677, Figure 6; pg. 5678, Figure 8). The engrafted cells migrated for a distance of 1-1.5 mm from the implantation sites (Abstract; pg 5674, col. 1, pgph 3) and expressed NGF (pg. 5674, col. 2, pgph 1). Finally, Martinez-Serrano et al. teaches that the cells expressed a transgene encoded NGF within 500 um of a target cell (pg 5675, Figure 4; pg 5676, Figure 5). Thus, by teaching all the limitations of the claims as written, Martinez-Serrano et al. anticipates the instant invention as claimed. As presently drawn Martinez-Serran anticipates the claims.

Applicant argues that the cited reference does not anticipate the claimed invention. However, applicant's arguments about the precise teachings of the cited reference in comparison with the teachings of the instant specification do not address the issue that the cited reference anticipates the claimed invention. Applicant's invention broadly encompasses any method of delivery of any neurotrophic transgene, which may be encoded by a viral vector into two or more cites in any mammalian brain, wherein the delivery sites are no more than 10 mm apart. It appears that applicant is contesting the validity of the examiners rejection based on limitations found in the specification that are not present in the claims. It is noted that for the purposes of rejections based on prior art, the art of record must only teach the limitations present in the claims. The reference of Martinez-Serrano et al. anticipates all of the limitations present in claims 1 and 2. The rejection is maintained for reasons of record as stated above and in the office actions of 1/19/05 and 9/08/05.

Continuation of 13. Other: :

It is noted that applicant has supplied an IDs for the references previously supplied on 7/19/05. Further a review of the record reveals that applicant properly filed an IDS on 7/19/05. Therefore these references will be listed on any patent resulting from this application. The finality of the previous action will not be withdrawn, because as previously stated in the action of 9/08/05: The references submitted with the reply were considered. The only issue was the appearance of said references on the face of any issued patent. This is not considered to be a reason for withdrawl of finality.

The prior Double patenting rejection over US Patent 6,451,306 is withdrawn in view of the terminal disclaimer filed by applicant.

Notice of Non-Compliant Amendment (37 CFR 1.121)	Application No. 10/748,337	Applicant(s) TUSZYNSKI, MARK H.	
	Examiner Louis D. Lieto	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

The amendment document filed on *08 November 2005* is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121. In order for the amendment document to be compliant, correction of the following item(s) is required.

THE FOLLOWING MARKED (X) ITEM(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

- ☐ 1. Amendments to the specification:
  - ☐ A. Amended paragraph(s) do not include markings.
  - ☐ B. New paragraph(s) should not be underlined.
  - ☐ C. Other _____.
- ☐ 2. Abstract:
  - ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
  - ☐ B. Other _____.
- ☐ 3. Amendments to the drawings:
  - ☐ A. The drawings are not properly identified in the top margin as "Replacement Sheet," "New Sheet," or "Annotated Sheet" as required by 37 CFR 1.121(d).
  - ☐ B. The practice of submitting proposed drawing correction has been eliminated. Replacement drawings showing amended figures, without markings, in compliance with 37 CFR 1.84 are required.
  - ☐ C. Other _____.
- ☒ 4. Amendments to the claims:
  - ☐ A. A complete listing of all of the claims is not present.
  - ☐ B. The listing of claims does not include the text of all pending claims (including withdrawn claims)
  - ☒ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified. Note: the status of every claim must be indicated after its claim number by using one of the following status identifiers: (Original), (Currently amended), (Canceled), (Previously presented), (New), (Not entered), (Withdrawn) and (Withdrawn-currently amended).
  - ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
  - ☒ E. Other: *(Previously Added) is improper. See claim 18.*

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP § 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf .

TIME PERIODS FOR FILING A REPLY TO THIS NOTICE:

1. Applicant is given **no new time period** if the non-compliant amendment is an after-final amendment or an amendment filed after allowance. If applicant wishes to resubmit the non-compliant after-final amendment with corrections, the **entire corrected amendment** must be resubmitted within the time period set forth in the final Office action.

2. Applicant is given **one month**, or thirty (30) days, whichever is longer, from the mail date of this notice to supply the **corrected section** of the non-compliant amendment in compliance with 37 CFR 1.121, if the non-compliant amendment is one of the following: a preliminary amendment, a non-final amendment (including a submission for a request for continued examination (RCE) under 37 CFR 1.114), a supplemental amendment filed within a suspension period under 37 CFR 1.103(a) or (c), and an amendment filed in response to a *Quayle* action.

   Extensions of time are available under 37 CFR 1.136(a) only if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action.

   Failure to timely respond to this notice will result in:
   Abandonment of the application if the non-compliant amendment is a non-final amendment or an amendment filed in response to a *Quayle* action; or
   Non-entry of the amendment if the non-compliant amendment is a preliminary amendment or supplemental amendment.